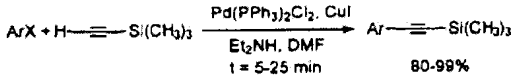
REMARKS

The presently claimed invention is drawn to a process for preparing organic alkynes. The process proceeds according to the following formula:

$$X\text{-Hal} + H\text{-}C{\equiv}C\text{-}Y \rightarrow X\text{-}C{\equiv}C\text{-}Y + H\text{-Hal}$$

The groups X and Y in the starting materials and products shown for the chemical equation above are "identical or different **organic** radicals."

The Office asserts that the presently claimed invention is anticipated by Erdelyi (*J. Org. Chem.*, 2001, 66, pp. 4165-4169). Erdelyi discloses the following chemical reaction:



The Office's assertion that the reaction of Erdelyi is the same as the reaction recited in present Claim 1 is not correct. The Office appears to be of the opinion that the chemical compound $H\text{-}C{\equiv}C\text{-}Si(CH_3)_3$ is the same as the group $H\text{-}C{\equiv}C\text{-}Y$ recited in the present claims. This is manifestly incorrect.

The group Y of the present claims is explicitly required to be an organic radical. In contrast, Erdelyi discloses the reaction of a silyl acetylene which has a **silyl** radical not the **organic** radical of present Claim 1 (i.e., the group Y). A silyl radical is not an organic radical.

Applicants submit it is readily recognized by those of ordinary skill in the art that an organic radical is a chemical moiety of formula $\cdot R$. Erdelyi does not disclose the reaction of an acetylenic material corresponding to the compound of formula (Ib) recited in present Claim 1 with an X-Hal compound of formula (Ia) as recited in present Claim 1. Instead, Erdelyi discloses the reaction of a compound having a silyl radical; namely, $\cdot Si(CH_3)_3$ with a compound of formula ArX. Silyl radicals are not organic radicals.

In Claim 1 of the present application the compound (Ib) has an acetylenic group (i.e.,-C≡C-) bonded to a hydrogen radical (i.e., -H) and an organic radical identified as "-Y". Therefore, compound (Ib) must contain at least one acetylenic carbon atom that is singly bonded to another carbon atom, i.e., the carbon of the organic radical. This condition cannot be met in the silyl acetylene disclosed in Erdelyi it, in contrast, contains one acetylenic carbon atom bonded to a hydrogen radical and another acetylenic carbon atom bonded to a silyl radical (i.e., $\cdot Si(CH_3)_3$).

The Office asserts that the group "Y" may be any organic group:

> Instant Y permits an organic group including those taught in Erdelyi et al.

See page 6, lines 7-8 of the July 29 Office Action.

This is not correct. The group Y must be an "organic radical". An organic radical necessarily bonds through a carbon atom. Erdelyi does not teach an acetylenic group bonded to an organic radical. Instead, Erdelyi describes an acetylenic group bonded to a silyl radical. As explained above, a silyl radical is not an organic radical and thus Erdelyi does not teach the present invention.

Applicants draw the Office's attention to page 3, line 39-page 10, line 4 which describes the group "Y" recited in present Claim 1. In every case the group "Y" is an organic radical singly bonded to an acetylenic group through a carbon atom.

The Office's rejection of the present claims as anticipated by Erdelyi is therefore not supportable and the rejection should be withdrawn.

In the alternate to anticipation, the Office asserts that the presently claimed invention is obvious over the combination of Erdelyi and Wang (*J. Chem. Research*, 2000, pp. 536-537). The Office's rationale for the rejection of the present claims as obvious over the combination of Erdelyi and Wang is in conflict with the Office's assertion that the present

claims are anticipated by Erdelyi. For example, the Office admits that Erdelyi does not teach the use of alkyl halides for the coupling process (see page 7, lines 15-16 of the July 29 Office Action). The Office provides no explanation of this conflict. If, as admitted by the Office, Erdelyi does not disclose the use of alkyl halides in coupling processes, how can Erdelyi anticipate claims which require the reaction of an organic halogen compound of formula X-Hal with an organic terminal alkyne?

Irrespective of the Office's erroneous rejection of the claims as anticipated by Erdelyi, the rejection of the claims as obvious over the combination of Wang and Erdelyi is legally not supportable.

For example, the Office asserts that Wang discloses "copper catalyzed cross coupling of alkynes under microwave irradiation, which includes instant process and compounds" (see page 7, lines 17-18 of the July 29 Office Action). This is not correct. Wang discloses the "copper-catalyzed cross coupling of aryl **iodi[d]es**" (see the Abstract of Wang). In contrast, present Claim 1 states that the halides are chloride and/or bromide, not iodide.

The Office alternately asserts that "analogous starting materials and reactants react similarly in view of the combine[d] teaching of the prior art" (see page 8, lines 1-3 of the July 29 Office Action). The Office's assertion that the starting materials of the presently claimed invention are analogous to the starting materials of Wang in combination with Erdelyi is not correct.

As already pointed out above, Erdelyi discloses the use of silyl acetylenes and Wang discloses the use of aryl iodides. Each of these starting materials is different from the starting materials recited in the present claims; namely, organic acetylenes and e.g., aryl chlorides and bromides. The compounds recited in the present claims are not analogous or homologous to the compounds of Erdelyi and Wang. Instead, the compounds recited in the present claims

include different chemical elements and are not otherwise structural isomers of the chemical groups disclosed in Erdelyi and Wang.

In short, the chemical reactions described in Erdelyi and Wang are entirely different from the chemical reaction recited in the present claims. The Office fails to set forth any reasonable or technical basis for modifying the reaction of Erdelyi in the manner of Wang. This is an especially noteworthy omission in view of the fact that an entirely different starting material is used in Erdelyi that is nowhere disclosed or suggested in Wang. Erdelyi and Wang are processes that undergo bond connectivity changes between different types of atoms. The Office fails to provide any reason why one would expect the substitution of different chemical reagents to provide the same result.

Applicants again point out that the original specification discloses that it was conventionally believed that aryl chlorides and aryl bromides cannot react in the manner of iodides in the reaction recited in the present Claim 1. In fact, Applicants explicitly distinguished the presently claimed invention from Wang;

> A distinct reduction in the reaction time can be achieved by carrying out the reaction under the action of microwave radiation.
>
> For instance, J.-X. Wang et al. (J. Chem. Research (S), 2000, p. 536-537) describe reactions of different terminal alkynes with organic iodine compounds in the presence of copper(I) iodide/triphenylphosphine and potassium carbonate in dimethylformamide (DMF). The comparison of the reactions show in table 2 of this publication, on the one hand under reflux of DMF, and on the other hand under the action of a microwave radiation source having an output of 375 W shows impressively that when comparable yields are obtained, the reactions in the latter case proceed more quickly than in the former case by factors of from 48 to 144.

See page 1, lines 27-41 of the present specification.

Moreover, Applicants pointed out that those of ordinary skill in the art would recognize that reactions that occur for iodine-substituted materials do not necessarily occur for chlorine- and bromine-substituted compounds:

> Investigations of solvent-free reactions of aryl, heteroaryl and vinyl iodides with terminal alkynes in the presence of palladium/copper(I) iodide/triphenylphosphine and potassium fluoride supported on aluminum oxide under the action of microwave radiation have been carried out by G. W. Kabalka et al. (Tetrahedron Lett. 41, 2000, p. 5151-5154). The authors mention (p. 5152) that aryl chlorides and bromides did not react and that the starting materials were recovered unchanged.
>
> We have now been found that, surprisingly, organic chlorine and bromine compounds can be reacted with terminal organic alkyne compounds to give alkyne derivatives in good to very good yields.

See page 1, line 43 through page 2, line 7 of the present specification.

Applicants submit that Kabalka makes it clear that it was conventionally thought that chlorides and bromides do not react to terminal alkynes in the same way as iodides. Kalbalka goes so far as to state that chloro- and bromo-organics do not react at all with terminal alkynes. Applicants submitted a copy of the Kabalka reference (*Tetrahedron Lett.*, 41, 2000, pp. 5151-5154) with the amendment filed on July 24, 2007.

Applicants submit that the evidence of record, e.g., Kabalka, is probative of the patentability of the presently claimed subject matter. Those familiar with Kabalka would have no reason to believe the reaction recited in the present claims would proceed. In fact, Kabalka makes it clear that iodine-substituted compounds may react with certain acetylene-type materials but that chlorine- and/or bromine-substituted materials will not undergo this reaction.

Applicants have shown, to the contrary, that such reactions can occur under the conditions recited in the present claims.

The rejection of the present claims as obvious over the combination of Erdelyi and Wang should be withdrawn at least because, *inter alia*, (i) the compounds of Erdelyi and Wang are not homologous with the compounds recited in the present claims and (ii) the evidence of record shows that those of ordinary skill in the art would have no reason to believe that chlorine- and bromine-substituted materials could undergo the same reactivity shown for iodine substituted materials.

As further support for the unobviousness of the presently claimed invention applicants submit herewith three publications as evidence that those of skill in the art recognize that the cross coupling reaction of an organic halide and a terminal alkyne proceeds differently for bromo- and chloro-substituted organic halides in comparison to iodo-substituted organic halides (see Chinchilla (i.e., R. Chinchilla and C. Najera in Chem Rev., 2007, 107, 874-922);[1] Thorand (S. Thorand and R. Krause, J. Org. Chem., 1998, 63, 8551-8553); and Tykwinski (R.R. Tykwinski, Angew. Chem., Int. Ed., 2003, 42, 1566-1568). Each of the Chinchilla, Thorand, and Tykwinski references distinguishes the Sonagashira cross-coupling reactions of chloro- and bromo-substituted organics from iodo-substituted organics (see the paragraph bridging the columns on page 875 of Chinchilla, the paragraph bridging the columns on page 8551 of Thorand, and the last full paragraph in the left column of page 1568 of Tykwinski). In fact, Tykwinski even discloses that the function of the presently claimed process (i.e., a process for preparing organic alkyne compound of formula X-C ≡C-Y by reacting an organic terminal alkyne of formula H-C ≡C-Y with X-Hal where Hal is chlorine or bromine) is "the Holy Grail of the Sonogashiri reaction" (see the last full paragraph in the left column of page 1568 of Tykwinski).

[1] The Chinchilla reference is not prior art to the present application.

Applicants submit that the evidence now of record in the present application demonstrates that the features of the presently claimed invention are probative of the non-obviousness of the presently claimed invention.

Applicants request withdrawal of the rejection of the claims as anticipated over Erdelyi and obvious over Erdelyi in combination with Wang.

The July 29 Office Action maintains the rejection of the claims for lack of enablement. Applicants submit that the Office's analysis of the Wands factors is nearly incomprehensible and fails to set forth any reasoned technical basis in support of the rejection. Instead, the Office's rejection is nothing more than a conclusory statement that ignores the evidence of record and ignores Applicants' previous arguments in support of patentability.

For example, the Office's analysis of Wands factors two and three makes no sense:

> Hence the processes applied to the above-mentioned compounds claimed by the applicant is not an art-recognized process and hence there should be adequate enabling disclosure in the specification with working example(s).
>
> ...
>
> Examples illustrated in the experimental section or written description offer no guidance or teachings as to how to perform the process of making compound of Formula I where X is phenyl, Y is phenyl.
>
> ...
>
> Although examples in the specification show the process, they are limited to X is phenyl, Y is phenyl with copper compound. There are no representative examples showing the viability of the process for X and Y or any radical with various substituents and metal compound embraced in the instant claims.

See pages 3 and 4 of the July 29 Office Action.

Not only is the above-quoted text from the Office Action nearly incomprehensible, it is contradictory on its face. In the second of the three above-quoted paragraphs the Office asserts that the examples "offer no guidance" whereas in the last of the above-quoted paragraphs the Office admits that the examples "show the process" when X and Y are phenyl.

The Office can't have it both ways; the Office cannot assert on the one hand that there is no guidance and on the other hand admit that there is guidance.

The Office's analysis of the remaining Wands factors is similarly flawed and represents nothing more than conclusory statements without any technical or legal basis for the rejection.

Applicants thus submit that the rejection of the claims for lack of enablement is not supportable and should be withdrawn.

It appears that the Office is of the belief that those of skill in the art would not be able to carry out the claimed invention for the entire range of compounds encompassed by the present claims. The Office further appears to be of the belief that the specification must include further examples to provide guidance to those of skill in the art how the reactions can be undertaken with starting materials other than those already exemplified in the specification.

Applicants submit that the evidence of record shows that those of ordinary skill in the art know how to carry out certain alkyne coupling-type reactions over a broad range of different starting materials. For example, Erdelyi shows that the prior art reaction proceeds when ArX includes aryl groups as diverse as aniline, anisole, benzene, pyridine, thiophene and benzoate. The groups disclosed in Erdelyi are aryl groups that are substituted with a number of hetero atoms, including sulfur and nitrogen, but are still able to proceed in the reaction described in the Erdelyi publication. Erdelyi therefore provides evidence that those of ordinary skill in the art know how to carry out acetylene coupling-type reactions using different starting materials and thus undue experimentation would not be required to carry out the scope of the presently claimed invention.

The Office fails to address this evidence. The Office's failure to address the evidence of record and provide a reasoned technical basis for supporting the rejection is legal error and thus the rejection should be withdrawn.

Furthermore, the Office blindly applied the lack of enablement rejection to Claims 17-20 added in the Amendment filed in the present application on April 23, 2008. It appears that the Office gave absolutely no consideration whatsoever to the subject matter of the new dependent claims. New dependent Claim 20 recites particular X and Y groups (i.e., benzoic acid and phenyl groups, respectively) and a particular metal compound, a particular base, a particular solvent, and a particular catalyst (i.e., copper (I) iodide, potassium carbonate, DMF, and triphenylphosphine, respectively). How can the subject matter of Claim 20 lack enablement when such a process is explicitly exemplified on pages 11 and 12 of the specification? New dependent Claims 17-19 likewise further identify the groups and conditions of the reaction recited in the present Claim 1. *Arguendo*, even if Claims 1-16 are in fact not enabled, an assertion to which Applicants do not agree, the subject matter of Claims 17-20 should be found commensurate in scope with the examples of the specification and thus enabled.

Thus, the rejection of Claims 1-20 for lack of enablement is both legally and technically not supportable and the rejection should be withdrawn.

For the reasons discussed above in detail, Applicants submit the rejection of the present claims as anticipated, obvious and lacking enablement should be withdrawn. Applicants request the mailing of a Notice of Allowance acknowledging the patentability of the presently claimed subject matter.

Respectfully submitted,

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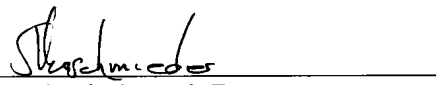

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